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UNITED STATES PATENT AND TRADEMARK OFFICE
BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES

EYAL **RAZ**
Junior Party
(U.S. Patent 6,498,148),

v.

ARTHUR M. **KRIEG** AND JOEL KLINE
Senior Party
(U.S. Application 09/337,584).

Patent Interference No. 105,526 (MPT)
(Technology Center 1600)

Before: JAMES T. MOORE, *Vice Chief Administrative Patent Judge* and SALLY LANE and MICHAEL P. TIERNEY, *Administrative Patent Judges*.

TIERNEY, *Administrative Patent Judge*.

MEMORANDUM OPINION and ORDER
Decision on Motions

This interference is before a motions panel for a decision on preliminary motions. An oral argument took place in this interference, a transcript of which appears in the record. (Paper 197). Representing Junior Party Raz was Oliver Ashe, Jr. Senior Party Krieg was represented by Lawrence Green.

I. Introduction

This interference is directed to a method for treating asthma comprising administering an effective amount of an immunostimulatory polynucleotide.

As stated by Raz, asthma is an inflammatory disorder that is characterized by inflamed airway passages, which causes shortness of breath. The most common type of asthma is allergic asthma, which refers to asthma triggered by an antigen. An immune response to an antigen generally involved two types of T helper cells, T helper 1 (Th1) and T helper 2 (Th2). Asthma and allergy generally involve a Th2 immune response. Immunostimulatory sequences (ISS) may be capable of shifting an immune response from a Th2 response to a Th1 response, which would reduce or suppress allergic inflammation. (Raz Motion 1, Paper 45, p. 5, l. 14 to p. 6, l. 9).

There are twelve (12) motions awaiting decision. Raz filed seven motions and Krieg five motions.

Raz filed a motion for judgment against Krieg based on lack of written description and/or enablement. Raz also filed a motion for judgment based on prior art alleging that Krieg is not entitled to 35 U.S.C. § 120 benefit due to a lack of written description and/or enablement. Further, Raz filed a motion for judgment that Raz's claims do not interfere-in-fact with Krieg's. We deny Raz's motions for judgment.

Krieg filed a motion for judgment that all of Raz's involved claims are unpatentable for lack of written description and/or enablement. We grant Krieg's motion as Raz's claims encompass the use of immunostimulatory plasmids, the use

of which was, and remains, unpredictable.

Raz filed a responsive motion requesting that the Board exercise its discretion and redeclare the interference to include a new Raz application and claim and substitute a count in the event that all of Raz's claims be held unpatentable. On this record, Raz has demonstrated that its new claim is patentable to Raz and interferes-in-fact with Krieg. As all of Raz's presently involved claims are unpatentable to Raz and as Raz has requested an interference with a new application and count, we enter judgment against Raz's involved claims and exercise our discretion to authorize the declaration of a new interference between Raz's additional application and Krieg's involved '584 application.

The remaining motions are dismissed as moot as they request judgment against Raz's already unpatentable claims, seek to designate claims as corresponding to the present count, have contingencies that did not come to pass, or seek to exclude evidence we have not relied upon.

II. Findings of Fact

The following findings of fact are believed to be supported by a preponderance of the evidence. To the extent that a finding of fact is a conclusion of law, it may be treated as such. Additional findings, as necessary, may appear in the Discussion portion of the opinion.

A. The Real Parties in Interest

1. Junior Party Raz

1) The Regents of the University of California is the real party in interest in Raz's involved U.S Patent 6,498,148. (Raz Real Party in Interest, Paper 10).

2. Senior Party Krieg

2) Krieg's involved U.S. Application 09/337,584 has been assigned to the University of Iowa Research Foundation and the United States of America as represented by the Secretary, Department of Health and Human Services. (Krieg Real Party in Interest, Paper 5).

B. Accorded Priority Benefit

1. Junior Party Raz

3) Raz is involved in the interference based upon U.S. Patent 6,498,148, issued December 24, 2002, filed January 21, 1999. (Notice Declaring Interference, Paper 1, p. 3).

4) Raz has been accorded an earlier constructive reduction to practice (*i.e.*, benefit for the purpose of priority) based on the following application:

i) U.S. Application 08/927,120, filed September 5, 1997. (Redeclaration, Paper 22).

1. Senior Party Krieg

5) Krieg is involved in the interference based upon U.S. Application 09/337,584, filed June 21, 1999. (Paper 1, p. 3).

6) Krieg has been accorded an earlier constructive reduction to practice (*i.e.*, benefit for the purpose of priority) based on the following applications:

i) U.S. Application 08/960,774, filed October 30, 1997, now U.S. Patent 6,239,116, issued May 29, 2001;

ii) U.S. Application 08/738,652, filed October 30, 1996, now U.S. Patent 6,207,646, issued March 27, 2001.

(Redeclaration, Paper 22).

C. Count and Claim Correspondence

7) There is a single count in the interference, Count 1, which reads as follows:

A method for treating asthma according to Claim 17 of U.S. Patent 6,498,148 or claim 44 of U.S. Application 09/337,584.

(*Id.*).

8) Raz '148 claim 17 depends from Raz claim 1. Raz claims 1 and 17 read as follows:

> 1. A method for treating asthma, comprising: administering to a mammal sensitized to an asthma-stimulating antigen an immunostimulatory polynucleotide comprising an immunostimulatory sequence (ISS), wherein the ISS comprises the sequence 5'-cytosine guanine-3', wherein the immunostimulatory polynucleotide does not comprise a nucleotide sequence encoding the antigen, and wherein the immunostimulatory polynucleotide is administered without the antigen, including without a polynucleotide encoding the antigen, and in an amount sufficient to treat asthma.
>
> 17. The method of claim 1, wherein the ISS is at least six nucleotides in length.

(Raz Clean Copy of Claims, Paper 8).

9) Krieg '584 claim 44 reads as follows:

> A method for treating asthma in a subject, comprising administering to an asthmatic subject an effective amount for treating asthma in the subject of an immunostimulatory nucleic acid, having a sequence including at least the following formula:

5' X_1 X_2 CGX_3 X_4 3'

wherein C is unmethylated, wherein X_1X_2 and X_3X_4 are nucleotides, wherein the nucleic acid has a length of 8 to 100 nucleotides.

(Krieg Clean Copy of Claims, Paper 3).

10) The claims of the parties are:

Krieg '584:	42-47, 49-53, 56-57, 82-85, 90, 92, 94, 96, 98, 100, 102-103
Raz '148:	1-19

(Paper 22, p. 2).

11) The claims of the parties that correspond to Count 1 are:

Krieg '584:	42-45, 47, 49-53, 57, 90, 92, 94, 96, 98, 100, 102-103
Raz '148:	1-4 and 6-19

(*Id.*)

12) The claims of the parties that do not correspond to Count 1 are:

Krieg '584: 46, 56, 82-85

Raz '148: 5

(*Id.*).

D. One of Ordinary Skill in the Art

13) The art in this interference relates to the field of immunology, in particular allergic asthma therapy and manipulating immune responses through the use of an immunostimulatory sequence (ISS). (Declaration of Dr. Robert Schleimer, RX 2001, ¶ 15; Declaration of Dr. David M. Center, KX 1003, ¶ 10).

14) A person of ordinary skill in the immunological arts would have an advanced degree, M.D. or Ph.D., in immunology, molecular biology or similar discipline and several years of laboratory or clinical experience with immune responses and/or asthma. (*Id.* at ¶ 16 and KX 1003 at ¶ 10).

E. Testifying Expert Qualifications

We find that the following experts are sufficiently qualified to give testimony with respect to the particular facts and techniques known by one of ordinary skill in the field of immunology and in particular, allergic asthma therapy.

1. Raz's Expert – Dr. Robert Schleimer (RX 2001)

15) Dr. Schleimer received a Ph.D. in Pharmacology and Toxicology from the University of California, Davis in 1980. (RX 2001, ¶ 2).

16) Dr. Schleimer is presently a Professor of Medicine and Chief of the Allergy-Immunology Division at Northwestern University Feinberg School of Medicine. (*Id.* at ¶ 1).

17) Dr. Schleimer is said to be an expert on innate immune responses and their relationship to allergic disease and has investigated the mechanisms involved in allergic diseases such as asthma. (*Id.* at ¶ 3).

2. Krieg's Experts

a. Dr. David M. Center (KX 1003)

18) Dr. David Center received a medical degree from Boston University in 1972. (Center Curriculum Vitae, KX 1004).

19) Dr. Center has held numerous positions including Research Fellow in immunology at Harvard Medical Center from 1975-1978 as well as various academic appointments including Professor of Medicine at Boston University School of Medicine since 1989. (KX 1003, ¶ 2).

20) Dr. Center has received numerous honors and awards for his work and has been an Associate Editor, Editorial Board member and a primary reviewer for various journals concerning immunology and lungs, e.g., Journal of Immunology. (*Id.* at ¶¶ 3-4).

b. Dr. Barbara P. Wallner

21) Dr. Wallner received a Ph.D. in Biochemistry from the University of Illinois in 1980. (KX 1011, ¶ 2).

22) Dr. Wallner has worked in a variety of positions including the discovery and development of allergy and autoimmune therapeutics from 1992 as the Director of Biochemistry, Vice President of Preclinical Research and Vice President of Research at Immunologic Pharmaceuticals, Inc. (*Id.* at ¶ 4).

23) Dr. Wallner has received numerous awards and honors for her work and has been a member of the American Association of Immunologists since 1998. (*Id.* at ¶ 3).

III. Opinion

There are twelve pending motions. The rules authorize the Board to take up motions for decision in any order. 37 C.F.R. § 41.125(a). We elect to first consider Raz's motion for judgment that Krieg's claims lack sufficient written

description and/or enablement.

A. Raz Substantive Motion 1 for Judgment Based on Lack of Sufficient Written Description and/or Enablement

Raz Motion 1 requests that the Board enter judgment that all of Krieg's involved claims are unpatentable to Krieg for lack of written description and/or enablement under 35 U.S.C. § 112, 1st paragraph. (Paper 45). According to Raz, the breadth of Krieg's involved claims renders them unpatentable to Krieg as Krieg allegedly failed to describe and/or teach how to make and use a method of treating asthma absent the co-administration of an antigen. (*Id.* at p. 2, l. 13 to p. 3, l. 16). Krieg opposes. (Paper 98).

1. Burden of Proof

The rules provide for the following burden of proof:

> To be sufficient, a motion must provide a showing, supported with appropriate evidence, such that, if unrebutted, it would justify the relief sought. The burden of proof is on the movant.

37 C.F.R. § 41.208(b). For the motions before us, the burden of proof is by a preponderance of the evidence. The burden of showing something by a preponderance of the evidence simply requires the trier of fact to believe that the existence of a fact is more probable than its nonexistence before the trier of fact may find in favor of the party who carries the burden. *Concrete Pipe & Products of California, Inc. v. Construction Laborers Pension Trust for Southern California*, 508 U.S. 602, 622, 113 S. Ct. 2264, 2279 (1993). Yet, in rendering factual findings:

> . . . it is impermissible for the Board to base its factual findings on its expertise, rather than on evidence in the record, although the Board's expertise appropriately plays a role in interpreting record evidence.

Brand v. Miller, 487 F.3d 862, 869 (Fed. Cir. 2007).

2. Claim Construction

We construe the claims beginning with the plain language of the claims but look to the specification to determine whether the inventor specifically defined the terms in the claims or disavowed certain embodiments. *Phillips v. AWH Corp*, 415 F.3d 1303, 1316 (Fed. Cir. 2005) (en banc). In construing the claims the United States Patent & Trademark Office is tasked with interpreting claims as broadly as their terms reasonably allow as they would be understood by one of ordinary skill in the art, taking into account whatever enlightenment by way of definitions or otherwise may be afforded by written description contained in applicant's specification. *In re Morris*, 127 F.3d 1048, 1054-55 (Fed. Cir. 1997); *In re Zletz*, 893 F.2d 319, 321 (Fed. Cir. 1989) (Board erred in reading unwritten limitations into claims on appeal and stated that it was incorrect for the Board to construe claims narrowly, such as done in courts confronting issues of infringement and validity).

Each of Krieg's involved claims is directed to a method of treating asthma comprising administering an ISS to an asthmatic subject. Raz contends that Krieg's claims encompass two subgenuses:

1) Co-administration of an ISS and antigen; and

2) Administration of an ISS without co-administration of an antigen.

(Paper 45, facts 6 and 7). Raz contends however, that specification fails to provide a sufficient written description and/or enablement for administering ISS without an antigen. (Paper 45, p. 3, ll. 4-11).

Krieg admits that its involved claims encompass a method of treating asthma wherein an antigen is co-administered with the CG nucleic acid (ISS) as well as methods wherein an antigen is not co-administered with the CG nucleic acid.

(Paper 98, p. 1, ll. 6-9 and admitting facts 6 and 7).

We agree with the parties that Krieg's claims encompass administration of an ISS with or without co-administration of the antigen. Specifically, the plain language of Krieg's claims does not require the co-administration of the antigen. Further, as discussed in detail below, Krieg's specification does not limit Krieg's invention to co-administration of the ISS and antigen. Accordingly, the parties' agreed upon construction is the broadest reasonable construction of the claims taken in light of Krieg's specification.

3. Written Description and Enablement

a. Principles of Law

While the specifics of the cases concerning adequate written description vary, the cases agree that the inquiry is factual and must be assessed on a case-by-case basis. Moreover, because of the fact-sensitive nature of the written description inquiry, the Federal Circuit has advised against misapplication of precedent in this area. *See, Union Oil Co. of California v. Atlantic Richfield Co.*, 208 F.3d 989, 1000 (Fed. Cir. 2000).

The purpose of the written description requirement is to clearly allow persons of ordinary skill in the art to recognize that the inventor invented what is claimed. *In re Gosteli*, 872 F.2d 1008, 1012 (Fed. Cir. 1989). Thus, the question is whether the specification "reasonably conveys" to a person skilled in the art that the inventor had possession of the claimed subject matter. *Bilstad v. Wakalopulos*, 386 F.3d 1116, 1126 (Fed. Cir. 2004). The inventor can reasonably convey possession by such descriptive means as words, structures, figures, diagrams, formulas, etc., that fully set forth the claimed invention. *Lockwood v. American Airlines, Inc.*, 107 F.3d 1565, 1571-72 (Fed. Cir. 1997).

To comply with the enablement requirements of 35 U.S.C. § 112, first paragraph, a specification must adequately teach how to make and how to use a claimed invention throughout its scope, without undue experimentation. *Plant Genetic Systems N.V. v. DeKalb Genetics Corp.*, 315 F.3d 1335, 1339 (Fed. Cir. 2003). Naturally, the specification must teach those of skill in the art "how to make and how to use the invention as broadly as it is claimed." *In re Vaeck*, 947 F.2d 488, 496 (Fed. Cir. 1991).

There are a variety of factors which may be considered in determining whether a disclosure would require undue experimentation. These factors include: (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. *In re Wands*, 858 F.2d 731, 737 (Fed. Cir. 1988). Not all of these factors need be reviewed to determine enablement. *Amgen, Inc. v. Chugai Pharm. Co., Ltd.*, 927 F.2d 1200, 1213 (Fed. Cir. 1991) (noting that the Wands factors "are illustrative, not mandatory. What is relevant depends on the facts.").

Additionally, in analyzing the *Wands* factors, we are mindful that a patent specification need not teach, and preferably omits, what is well known in the art. *Spectra Physics Inc. v. Coherent Inc.*, 827 F.2d 1524, 1534 (Fed. Cir. 1987).

Compliance with 35 U.S.C. § 112, first paragraph is as of the filing date of the application relied on, not the filing date of an ancestor application. *Microsoft v. Reiffin*, 214 F.3d 1342, 1346 (Fed. Cir. 2000).

The filing date of the involved Krieg '584 application is June 21, 1999. (Paper 1, p. 3). Accordingly, the date for compliance with 35 U.S.C. § 112, 1st paragraph for Krieg's '584 application is **June 21, 1999**.

b. Findings of Fact

The following findings of fact present relevant highlights regarding Krieg's written description and enablement for its involved claims. The findings are supported by at least a preponderance of the evidence.

i. Krieg's Involved '584 Specification

24) Krieg's specification states that its field of the invention relates to oligonucleotide immunostimulatory sequences ("ISS") having at least one unmethylated CpG (cytosine-guanine) dinucleotide. (RX 2004, p. 2, ll. 14-16).[1]

25) Krieg's specification summarizes its invention as being based on the following understanding:

> The present invention is based on the finding that certain nucleic acids containing unmethylated cytosine-guanine (CpG) dinucleotides activate lymphocytes in a subject and redirect a subject's immune response from a Th2 to a Th1 (e.g., by inducing monocytic cells and other cells to produce Th1 cytokines, including IL-12, IFN-γ and GM-CSF). Based on this finding, the invention features, in one aspect, novel immunostimulatory nucleic acid compositions.

(*Id.* at p. 7, l. 31 to p. 8, l. 4).

26) Krieg's specification states that its nucleic acid sequences can be used to treat or prevent disorders, such as asthma. Specifically, Krieg states:

> The nucleic acid sequences of the invention can also be used to treat, prevent or ameliorate other disorders (e.g., a tumor or cancer or a viral, fungal, bacterial or parasitic infection). In addition, the nucleic acid sequences can be administered to stimulate a subject's response to

[1] The pages in Krieg's '584 specification were apparently renumbered by hand. For convenience we refer to the typewritten numbers appearing at the top of the page.

a vaccine. ***Furthermore, by redirecting a subject's immune response from Th2 to Th1, the claimed nucleic acid sequences can be used to treat or prevent an asthmatic disorder***. In addition, the claimed nucleic acid molecules ***can be*** administered to a subject in conjunction with a particular allergen as a type of desensitization therapy to treat or prevent the occurrence of an allergic reaction associated with an asthmatic disorder.

(*Id.* at p. 9, ll. 5-12, emphasis added).

27) The '584 specification defines allergy and asthma as follows:

> An "allergy" refers to acquired hypersensitivity to a substance (allergen). Allergic conditions include eczema, allergic rhinitis or coryza, hay fever, bronchial asthma, urticaria (hives) and food allergies, and other atopic conditions.
>
> "Asthma"--refers to a disorder of the respiratory system characterized by inflammation, narrowing of the airways and increased reactivity of the airways to inhaled agents. Asthma is frequently, although not exclusively associated with atopic or allergic symptoms.

(*Id.* at p. 13, ll. 26-31).

28) The specification further states that:

> In another aspect, the nucleic acid sequences of the invention are useful as an adjuvant for use during antibody production in a mammal. Specific, but non-limiting examples of such sequences include: TCCATGACGTTCCTGACGTT (SEQ ID NO: 10), GTCGTT (SEQ. ID. NO:57), GTCGCT (SEQ. ID. NO: 58), TGTCGCT (SEQ. ID. NO: 101) and TGTCGTT (SEQ. ID. NO: 102). ***Furthermore, the claimed nucleic acid sequences can be administered to treat or prevent the symptoms of an asthmatic disorder by redirecting a subject's immune response from Th2 to Th1.*** An exemplary sequence includes TCCATGACGTTCCTGACGTT (SEQ ID NO.10).

(*Id.* at p. 17, ll. 10-17, emphasis added).

29) The specification states that the nucleic acids of the invention may have significant therapeutic utility in treatment of asthma as follows:

> ***Nucleic acids containing unmethylated CpG motifs may also have significant therapeutic utility in the treatment of asthma.*** Th2 cytokines, especially IL-4 and IL-5 are elevated in the airways of asthmatic subjects. These cytokines promote important aspects of the asthmatic inflammatory response, including IgE isotype switching, eosinophil chemotaxis and activation and mast cell growth. Th1 cytokines, especially IFN-.gamma. and IL-12, can suppress the formation of Th2 clones and production of Th2 cytokines.
>
> As described in detail in the following Example 12, oligonucleotides containing an unethylated CpG motif (i.e., TCCATGACGTTCCTGACGTT; SEQ ID NO. 10), but not a control oligonucleotide (TCCATGAGCTTCCTGAGTCT; SEQ ID NO. 8) prevented the development of an inflammatory cellular infiltrate and eosinophilia in a murine model of asthma. Furthermore, the suppression of eosinophilic inflammation was associated with a suppression of a Th2 response and induction of a Th1 response.

(*Id.* at p. 53, l. 26 to p. 54, l. 5).

30) The specification defines an effective amount of its nucleic acid as follows:

> The term "effective amount" of a nucleic acid molecule refers to the amount necessary or sufficient to realize a desired biologic effect. . . . An "effective amount" for treating asthma can be that amount useful for redirecting a Th2 type of immune response that is associated with asthma to a Th1 type of response.

(*Id.* at p. 54, ll. 21-28).

31) Krieg's '584 specification does not contain an explicit statement that limits Krieg's method of treating asthma to the coadministration of an nucleic acid ISS and an antigen.

ii. Knowledge of One of Ordinary Skill in the Art and the State of the Art

Kline '96 & '97 Abstracts and '98 Article

32) Kline and others published an abstract in 1996 (RX 2008), an abstract in 1997 (RX 2009) and an article in 1998 (RX 2010).

33) The abstracts and article report the examination on the effects of ISS using a murine model of asthma. (RX 2001, ¶ 76).

34) Raz's expert, Dr. Schleimer, testifies that:

> One of ordinary skill in the art would have understood that the Kline '98 Paper described in a detailed manner the experiments depicted in the Kline '96 Abstract and the Kline '97 Abstract.

(*Id.*).

35) Dr. Schleimer, testifies that one of ordinary skill in the art reading Kline's abstracts and article would have been discouraged from administering ISS without co-administering antigen to treat asthma. Specifically, Dr. Schleimer states:

> Considering the Kline '96 and '97 Abstracts and the Kline '98 Paper, it would have been interpreted by one of ordinary skill in the art in 1996-1999 that ISS administered to a sensitized subject without co-administration of an antigen would not be effective in treating asthma. In fact, the Kline Abstracts and publications would have discouraged one of ordinary skill in the art from practicing a method of administering ISS, without co-administering antigen, to treat asthma.

(*Id.* at ¶ 106).

Broide '98 Article

36) In 1998 Broide and Raz, among others, authored an article reporting on ISS and its ability to significantly inhibit airway eosinophilia. (RX 2012, abstract).[2]

37) The Broide article provides the following statement under the heading "Discussion:"

> In this study, we demonstrate that ISS inhibits airway eosinophilia and prevents the development of airway hyperresponsiveness. ***These observations are similar to those noted by Kline et al. (20) [Kline's '98 article] in a different mouse model of airway inflammation. In the present study, we have extended these observations*** by demonstrating 1) the novel mechanism by which ISS inhibits airway eosinophilia through inhibition of the production and release of eosinophilia from the bone marrow; 2) that inhibition of bone marrow production of eosinophils was associated with a significant inhibition of IL-5, GM-CSF, and IL-3 production; 3) that ISS exerted this inhibitory effect on T cell cytokine production indirectly by stimulating monocytes/macrophages and NK cells to generate IL-12 and IFNs, as demonstrated in in vitro neutralizing Ab studies; 4) that the effect of ISS on reducing the number of tissue eosinophils was both immediate (onset within 1 day) and sustained (over 6 days), and was not due to ISS directly inducing eosinophil apoptosis; 5) that ISS was effective in inhibiting eosinophilic airway inflammation when administered either systemically or mucosally (i.e., i.n or i.t); 6) that a single administration of ISS (systemic or mucosal) inhibited airway eosinophilia as effectively as daily systemic administrations of corticosteroids for 7 days; and 7) that while both ISS and corticosteroids inhibited IL-5 generation, only ISS was able to induce IFN-γ (a cytokine that importantly biases the immune system to generate a Th1 and not a Th2 response to subsequently encountered allergens). Thus, systemic or mucosal administration of ISS before allergen exposure provides a novel form of active immunotherapy in

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[2] Broide *et al.*, "Immunostimulatory DNA Sequences Inhibit IL-5, Eosinophilic Inflammation, and Airway Hyperresponsiveness in Mice," *J. Immunol.* 161: 7054-7062 (1998) (RX 2012).

allergic diseases.

(RX 2012, p. 7059, col. 2 to 7060, col. 2).

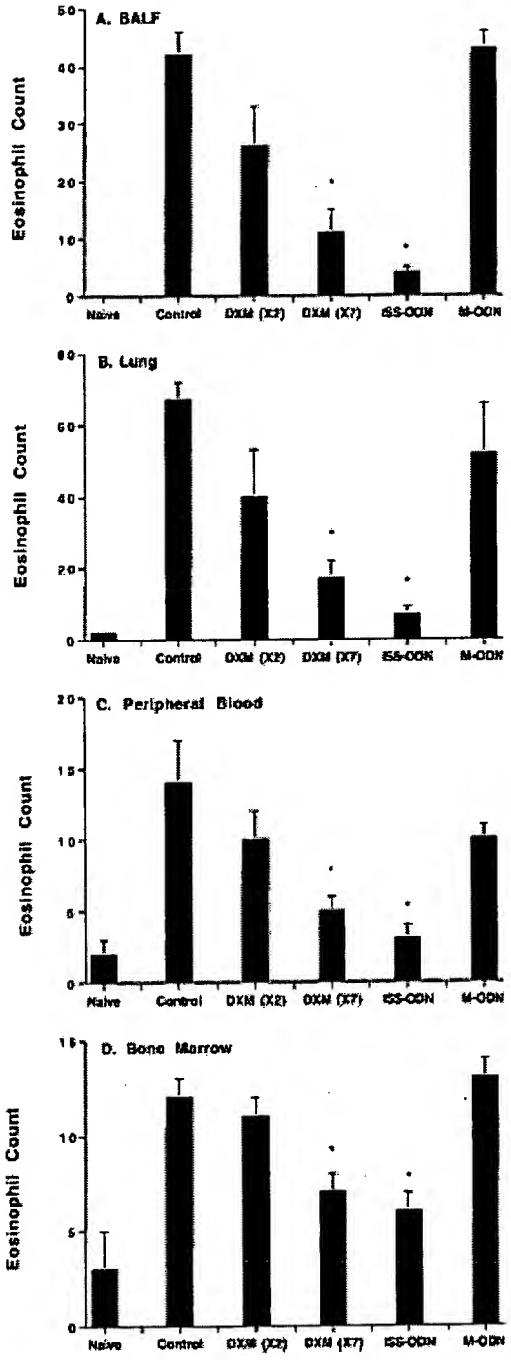
38) We credit Broide's contemporaneous statement that its observations are similar to those noted in Kline's 1998 article. (*Id.*).

39) We credit Broide's contemporaneous statement that its observations are an extension of those noted in the Kline '98 article. (*Id.*).

40) Raz's expert, Dr. Schleimer, testifies that Broide's 1998 article (RX 2012) investigated the administration of ISS-ODN alone, in the absence of antigen challenge, in a mouse model of asthma. (RX 2001, ¶¶ 92-93, citing RX 2012, abstract and p. 7058).

41) One of ordinary skill in the art would have known that high levels of eosinophil infiltration is indicative of asthma. (*Id.* at ¶ 49).

42) Figure 4 of Broide's 1998 article reports the effects of systemic ISS or corticosteroids on BALF, lung, blood and bone marrow eosinophil levels as follows in graphical format:



The levels reported above in Figure 4 are for groups of mice sensitized and challenged with an antigen (OVA) or OVA sensitized and pretreated with either ISS-ODN or M-ODN before the first OVA inhalation challenge. (*Id.* at p. 7060).

43) Broide demonstrates that ISS induced Th1 cytokine production and inhibited Th2 cytokine production and eosinophilic inflammation when ISS was administered before or co-administered with allergen challenge. (RX 2001, ¶ 94, citing RX 2012, p. 7059-7061).

44) Broide demonstrates that ISS can inhibit Th2 cytokines in the presence or absence of antigen challenge. (*Id.*).

45) Dr. Schleimer testifies that one of ordinary skill in the art would have considered it relevant that all of Broide's treatments with ISS were performed in mice that had been sensitized by repeated administration of antigen but Dr. Schleimer does further explain the relevancy of this testimony. (RX 2001, ¶ 95).

46) One of ordinary skill in the art in 1999 understood that an ISS can inhibit Th2 cytokines and airway eosinophilia in the presence or absence of antigen challenge. (Dr. Schleimer Declaration, RX 2001, ¶ 94, citing Broide '98 article, RX 2012).

c. Analysis of Krieg's Written Description

1. Krieg's '584 Specification Encompasses Methods of Treating Asthma Using ISS With or Without Co-administration of an Antigen

Raz contends that one of ordinary skill in the art would not have considered Krieg to be in possession of a method of treating asthma comprising administering an ISS without co-administration of an ISS. (Paper 45, p. 7, ll. 3-6). Raz summarizes its interpretation of Krieg's specification as follows:

Below, various portions of the Krieg Specification are considered. In

> certain instances, the Krieg Specification describes a method of treating or preventing asthma by co-administration of an ISS with an antigen. See, Facts 29 and 32. In other instances, the Krieg Specification generically refers to methods of treating or preventing asthma using an ISS, without reference to the presence or absence of an antigen. See, Fact 42. Significantly, there is not a single instance wherein the Krieg Specification describes a method of treating or preventing asthma comprising the administration of an ISS without co-administration of an antigen. See, Fact 22. Accordingly, one of ordinary skill in the art would not have considered the Krieg Specification to describe or enable a method of treating asthma by administering ISS without co-administering an antigen.

(Paper 45, ll. 7-15).

The plain language of Krieg's '548 specification does not limit Krieg's method of treating asthma to the co-administration of ISS and an antigen. For example, Krieg's specification provides the following statements:

> ***Furthermore, by redirecting a subject's immune response from Th2 to Th1, the claimed nucleic acid sequences can be used to treat or prevent an asthmatic disorder.*** In addition, the claimed nucleic acid molecules ***can be*** administered to a subject in conjunction with a particular allergen as a type of desensitization therapy to treat or prevent the occurrence of an allergic reaction associated with an asthmatic disorder. (RX 2004, p. 9, ll. 8-12, emphasis added).
>
> ***Furthermore, the claimed nucleic acid sequences can be administered to treat or prevent the symptoms of an asthmatic disorder by redirecting a subject's immune response from Th2 to Th1.*** An exemplary sequence includes TCCATGACGTTCCTGACGTT (SEQ ID NO:10). (*Id.* at p. 17, ll. 14-17, emphasis added).
>
> The term "effective amount" of a nucleic acid molecule refers to the amount necessary or sufficient to realize a desired biologic effect. . . . An "effective amount" for treating asthma can be that amount useful for redirecting a Th2 type of immune response that is associated with asthma to a Th1 type of response. (*Id.* at p. 54, ll. 21-28).

Krieg's specification, as evident from the passages above, contemplates the treatment of asthma by redirecting a subject's immune response from a Th2 to Th1 response. Krieg accomplishes this by administering an ISS to an asthma patient. The ISS "can" be administered in conjunction with an antigen, but "can" does not mean "must." Accordingly, Krieg teaches that the ISS "can be" administered in conjunction with an antigen but that the antigen is not required.

Raz's arguments against Krieg's possession are premised on the theory that treatment of asthma would involve the co-administration of an antigen. (Paper 45, p. 7, ll. 16-21). Based on this expectation, Raz argues that Krieg's statements of treating asthma using an ISS do not describe a specific method and therefore do not describe treating with ISS alone. (*Id.*, e.g., p. 8, l. 19 to p. 9, l. 9).

Raz's arguments do not demonstrate that the plain language of Krieg's specification fails to reasonably convey what it claims as its invention. Rather, Raz's arguments regarding what one of ordinary skill in the art would have expected at the relevant time are more akin to an attack on Krieg's utility, an issue that has not been explicitly argued on this record. Regardless, as explained below with respect to enablement, one of ordinary skill in the art in 1999 would have understood Krieg as teaching the use of a known class of compounds (ISS) in an known manner (administration to an asthmatic subject) to treat a known disorder (asthma). (See, Broide '98, RX 2012, Raz Reply 6, Paper 121, p. 3, ll. 11-21, p. 7, ll. 2-8). Accordingly, we find that Raz has failed to provide sufficient and credible evidence to demonstrate that Krieg lacks sufficient written description for its method of treating asthma with an ISS.

d. Enablement Analysis of Krieg's Disclosure

Raz contends that Krieg's involved claims are unpatentable because Krieg does not enable the full scope of the claimed invention. Specifically, Raz contends that Krieg does not teach how to make or use a method of treating an asthma using an ISS without the co-administration of an antigen. Raz does not contend that Krieg's specification lacks an enabling disclosure for treating asthma where an ISS and an antigen are co-administered. (See, e.g., Paper 45, p. 16, ll. 21-23).

Raz directs our attention to three of the eight *Wands* factors to support its position. (Paper 45, p. 15, l. 15-18). Specifically, Raz contends that the state of the art, the breadth of the claims and the lack of direction or guidance presented in the specification demonstrates that undue experimentation would be required to practice the full scope of Krieg's claims. (Paper 45, p. 15, l. 19 to p. 17, l. 12).

1. State of the Art in 1999: One of Ordinary Skill in the Art Understood that ISS's Can Inhibit Th2 Cytokines in Absence of Antigen Challenge

Raz directs our attention to Kline's '96 and '97 abstracts as well as Kline's '98 article as representative of the state of the art. According to Raz:

> One of ordinary skill in the art knowledgeable as to the state of the art in 1996-1998, as reported by Kline et al., would have understood that administration of ISS without co-administration of an antigen is ineffective in treating asthma.

(Paper 45, p. 16, ll. 17-19). The relevant date for the state of the art is June 21, 1999, the filing date of Krieg's '548 application and takes into account all the known prior art and is not limited to that reported by Kline. In particular, Raz's arguments regarding the state of the art fail to take into account Raz's own contemporaneous teachings.

Raz and Broide, among others, coauthored an article in 1998. (Broide '98,

RX 2012). The Broide '98 article investigated the administration of ISS-ODN alone in a mouse model of asthma (in the absence of antigen challenge). (Schleimer Declaration, RX 2001, ¶¶ 92, 93, citing RX 2012, abstract and p. 7058). As acknowledged by Raz's expert, "Broide reported that ISS can inhibit Th2 cytokines in the presence or absence of antigen challenge." (RX 2001, ¶ 94). Further, Raz's expert acknowledges that high levels of eosinophil infiltration are indicative of asthma and that Broide reports inhibiting eosinophilic inflammation using only an ISS. (*Id.* at ¶¶ 49, 94). Accordingly, one of ordinary skill in the art in 1999 understood that an ISS could treat asthma without the co-administration of an antigen.

Raz, and its expert, contend that one of ordinary skill in the art would have considered a method of treating asthma using an ISS without the co-administration of an asthma-stimulating antigen to be a significant achievement. (Paper 45, p. 7, ll. 16-21). Yet, Raz and its expert fail to reconcile this belief with Broide's '98 publication that teaches one of ordinary skill in the art to use an ISS to treat asthma without the co-administration of an antigen. Accordingly, we find that Raz has failed to demonstrate that the absence of the antigen was a significant achievement in 1999. Specifically, taking Broide' teachings into account, we find that one of ordinary skill in the art as of the relevant date would have known that an ISS could be used to treat asthma with or without the co-administration of an antigen.

Based on the record presented, we find that the level of skill in the art was high (M.D. or Ph.D. with several years of experience, RX 2001, ¶ 15), the state of the art was high (known to use ISS alone to treat asthma (RX 2012)), and the breadth of the claim was reasonable in light of the state of the art and level of skill. Raz is correct that Krieg's specification does not provide an example of treating asthma using an ISS without the co-administration but that this factor does not outweigh the high level of skill and state of the art. Balancing the *Wands* factors

we hold that Raz has failed to provide sufficient and credible evidence to support its contention that undue experimentation was required to make and use the portion of Krieg's claims that does not require the co-administration of an antigen.

Raz has not carried its burden of proof that Krieg's involved claims lack sufficient written description and/or enablement. Raz Motion 1 is therefore ***denied***.

We do not reach the issues and evidence presented in Krieg Opposition 1 or Raz Reply 1 as we have denied Raz Motion 1 for failing to make out a prima facie case and the Standing Order prohibits a party from presenting new issues or evidence in a reply that were necessary to make a prima facie case for the relief requested in the motion. (Standing Order "SO", Paper 2 at ¶ 122.5 and 37 C.F.R. § 41.122(b) "All arguments for the relief requested in a motion must be made in the motion. A reply may only respond to arguments raised in the corresponding motion.").

B. Raz Substantive Motion 3 for Judgment Based on Prior Art

Raz requests that Krieg's involved claims be held unpatentable under 35 U.S.C. § 102(b). According to Raz, Krieg's involved claims are not entitled to 35 U.S.C. §120 benefit of Krieg's earlier filed '652 and '774 applications. Raz states that, without §120 benefit, all of Krieg's involved claims would have been anticipated by Krieg's own WO 98/18810 publication. (Paper 50, p. 1, ll. 1-9). Krieg opposes. (Paper 102).

1. Legal Principles: 35 U.S.C. § 120

35 U.S.C. §120 benefit establishes an applicant's entitlement to a given date for purposes of determining the patentability of the applicant's *claims*. To obtain

benefit under §120, a party must establish that an earlier filed U.S. application satisfies the requirements of the first paragraph of 35 U.S.C. § 112, with respect to each claim for which benefit is desired. *Microsoft v. Reiffin*, 214 F.3d 1342, 1346 (Fed. Cir. 2000) ("Analysis of the disclosure in ancestor applications is appropriate when benefit of an earlier filing is sought under 35 U.S.C. §120"). Accordingly, while Raz raises arguments similar to those presented in Raz Motion 1, we review the written description and enablement arguments with respect to Krieg's earlier filed '652 application, filed October 30, 1996, and '774 application, filed on October 30, 1997.

2. Findings of Fact

The following findings of fact present relevant highlights regarding Krieg's written description and enablement for its involved claims in light of the '652 and '774 applications. The findings below are in addition to those discussed elsewhere in this decision and are supported by at least a preponderance of the evidence.

47) Krieg's involved '584 application is a divisional of Krieg '774, and Krieg's '774 application is a continuation-in-part of Krieg's '652 application. (RX 2004, p. 1, ll. 4-5).

a. Krieg's '774 Application (RX 2005)

48) The '584 application is a divisional of the '774 application and for all relevant purposes appears to contain the same disclosure relating to the treatment of asthma with a nucleic acid sequence. For example, the following statements appear in both Krieg '774 and '584:

> Furthermore, by redirecting a subject's immune response from Th2 to Th1, the claimed nucleic acid sequences can be used to treat or prevent an asthmatic disorder. In addition, the claimed nucleic acid molecules ***can be*** administered to a subject in conjunction with a particular allergen as a type of desensitization therapy to treat or prevent the occurrence of an allergic reaction associated with an asthmatic disorder. (RX 2004, p. 9, ll. 8-12, RX 2005, p. 10, ll. 18-22, emphasis added to quotation).
>
> Furthermore, the claimed nucleic acid sequences can be administered to treat or prevent the symptoms of an asthmatic disorder by redirecting a subject's immune response from Th2 to Th1. An exemplary sequence includes TCCATGACGTTCCTGACGTT (SEQ ID NO:10). (RX 2004, p. 17, ll. 14-17, RX 2005, p. 20, ll. 12-14).

49) Like Krieg '584, Krieg '774 Example 12 reports that the co-administration of an ISS and an antigen exhibited a reduced immune response after airway challenge with SEA. (*Id.* at p. 78, ll. 15-17).

b. Krieg's '652 Application (RX 2006)

50) Krieg's '652 specification uses slightly different language than the '774 and '584 applications to describe treating asthma with an ISS.

51) For example, Krieg's '652, states:

> Further, by redirecting a subject's immune response from Th2 to Th1, the instant claimed nucleic acid molecules can be administered to treat or prevent the symptoms of asthma. In addition, the claimed nucleic acid molecules can be administered in conjunction with a particular allergen to a subject as a type of desensitization therapy to treat or prevent the occurrence of an allergic reaction.

(RX 2006, p. 8, ll. 13-17, compare with RX 2004, p. 9, ll. 8-12, RX 2005, p. 10, ll. 18-22, emphasis added to quotation).

52) Krieg's '652 application, like the '584 and '774 applications, states:

> Nucleic acids containing unmethylated CpG motifs may also have significant therapeutic utility in the treatment of asthma. Th2 cytokines, especially IL-4 and IL-5 are elevated in the airways of asthmatic subjects. These cytokines promote important aspects of the asthmatic inflammatory response, including IgE isotype switching, eosinophil chemotaxis and activation and mast cell growth. Th1 cytokines, especially IFN-.gamma. and IL-12, can suppress the formation of Th2 clones and production of Th2 cytokines.

(RX 2006, p. 41, ll. 31-36, RX 2005, p. 66, ll. 10-15 and RX 2004, p. 53, l. 26 to p. 54, l. 5).

c. State of the Art

Sato

53) In July 1996, Sato and Raz, among others,[3] reported that a characteristic of ISS molecules is that they are capable of shifting an immune response from a Th2 response to a Th1 response. (Schleimer Declaration, RX 2001, ¶¶ 53-55, Sato, RX 2007).

Kline '96 Abstract

54) Kline *et al.* published an abstract in September 1996 entitled "CpG Motif Oligonucleotides are Effective in Prevention of Eosinophilic Inflammation in a Murine Model of Asthma." (RX 2008).

55) The '96 abstract reports that when ISS is co-administered with an antigen (i.e., Schistosome eggs), immune response to subsequent SEA airway challenge

[3] Sato *et al.*, "Immunostimulatory DNA Sequences Necessary for Effective Intradermal Gene Immunization." *Science* 273: 352-354 (July 19, 1996).

was reduced. (RX 2001, ¶ 60).

56) The '96 abstract provides the following statement:

> Systemic administration of the oligonucleotide TCCATGACGTTCCTGACGTT, alone did not result in any significant change in BAL cellularity, but when this oligonucleotide [c]ontaining the CpG motif was administered simultaneously with the schistosome eggs, airway eosinophilia was significantly decrease (to 7 +/- 5%); moderate BAL lymphocytosis (23 +/- 10%) was also induced.

(RX 2008).

57) The meaning of Kline's '96 abstract regarding administration of the oligonucleotide alone is open to interpretation. (RX 2001, ¶¶ 62-63).

58) For example, Kline's '96 abstract could mean that the injected ISS composition did not elicit an immune response in the mouse, i.e., a control. (*Id.*).

Kline '97 Abstract

59) Kline *et al.* published an abstract in March 1997 entitled "Immune Redirection by CpG Oligonucleotides: Conversion of a Th2 Response to a Th1 Response in a Murine Model of Asthma," J. Investig. Med. 45(3): 282A (March 1997) (RX 2009).

60) The '97 abstract reports that the co-administration of an ISS and an antigen reduced the immune response to subsequent antigen challenge. (RX 2001, ¶ 70).

61) Kline's '97 abstract contains the following statement:

> In addition to prevention of sensitization, CpG ODN co-administered with schistosome eggs (but not CpG ODN alone) lead to decreased airway eosinophilia following subsequent airway challenge with SEA.

(RX 2009).

62) One of ordinary skill in the art would have considered the above passage to be ambiguous with respect to the experimental design and open to interpretation. (RX 2001, ¶¶ 72-74).

63) One interpretation is that the CpG ODN (ISS) was administered alone refers to a control group to demonstrate that the CpG ODN did not appear to effect airway eosinophilia. (RX 2001, ¶ 73).

Kline '98 Article

64) Kline and Krieg, among others, published an article in 1998 entitled "Cutting Edge: Modulation of Airway Inflammation by CpG Oligodeoxynucleotides in a Murine Model of Asthma," *J. Immunol.* 160:2555-2559 (January 14, 1998). (RX 2010).

65) Kline's 98 article reports that unmethylated CpG ODN can prevent allergen-induced airway inflammation in previously sensitized mice and that CpG DNA may protect against asthma. (*Id.*, abstract).

66) The article reports testing four sets of conditions:

1) mice sensitized with Schistosome eggs followed by airway challenge with SEA (Egg/SEA);

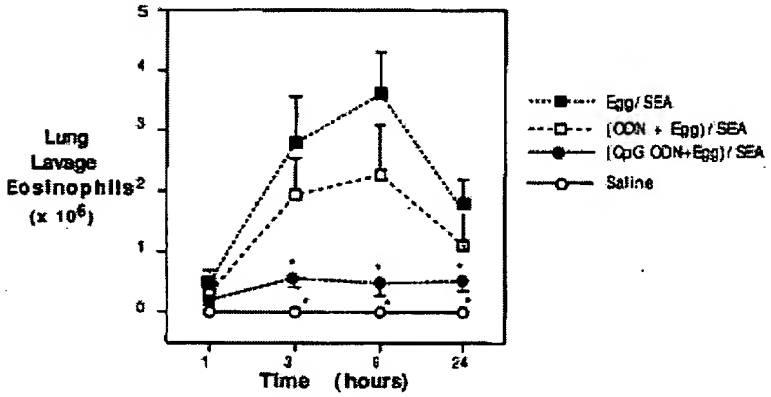
2) mice given co-administration of ODN and Schistosome eggs followed

by the airway challenge with SEA (ODN + Egg)/SEA;

3) mice given co-administration of ISS (CpG ODN) and Schistosome eggs and then challenged with SEA (CpG OND + Egg)/SEA; and

4) mice given saline alone and subsequently challenged with saline (Saline).

67) Figure 1 of Kline's 98 article graphically depicts the data from the above testing:



The above depiction shows that CpG ODN and eggs decreased the eosinophil counts as compared to eggs or ODN and eggs. (RX 2010, RX 2001, ¶ 80).

68) Kline's '98 article also reports that:

> Down-regulation of Ag-driven Th2-mediated responses following sensitization is an important therapeutic goal. To investigate whether CpG DNA may overcome a preexisting Th2 response, we examined the effect of CpG ODN on eosinophilic airway inflammation in mice sensitized to SEA. All mice received schistosome eggs, were reexposed to eggs in the presence of CpG or control ODN or no ODN (day 7), and then were studied following two SEA inhalation challenges (days 14 and 21). Mice given schistosome eggs without ODN developed marked airway eosinophilia (2.91 +/- 0.70 x 10^6 cells). In contrast, the mice that received CpG ODN along with eggs

(day 7) developed significantly less airway eosinophilia (0.28 + /- 0.14 x 10^6 cells, $p < 0.01$), but the mice that received control ODN and eggs (day 7) developed eosinophilia similar to that of the mice that received schistosome eggs alone (Fig. 5).

These findings demonstrate that the schistosome/SEA model of asthma is characterized by IgE production, airway eosinophilia, pulmonary IL-4 secretion, and bronchial hyperreactivity, which do not develop if CpG ODN are coadministered along with the schistosome eggs. ***CpG ODN alone do not offer significant protection against the development of airway inflammation***. In addition these effects are Ag specific; in other studies (not shown), CpG ODN can protect against the development of eosinophilic airway inflammation in an OVA murine model of asthma, but protection against OVA sensitization does not confer protection against schistosome sensitization.

(RX 2010, p. 2557, col. 1 last ¶ to p. 2558, 1st ¶).

69) Raz's expert, Dr. Schleimer, testifies that there is no data in Kline's '98 article to provide context for Kline's statement that CpG ODN does not offer significant protection. (RX 2001, ¶ 83).

70) For example, Dr. Schleimer testifies that the statement could be a reference to controls where a CpG ODN was administered to non-sensitized mice without co-administration of an antigen. (*Id.*).

71) Dr. Schleimer testifies that, even under various interpretations, Kline's '98 article does not demonstrate possession of a method of treating asthma wherein an ISS is administered without co-administration of an antigen. (*Id.*).

3. Krieg's Written Description for the '652 and '774 Applications

a. The Plain Language of the '652 and '774 Applications

Krieg's involved claims are directed to a method for treating asthma comprising administering an ISS. The USPTO provides claims with their broadest reasonable interpretation *consistent with the specification*. *Morris* at 1054-55. Raz contends that the broadest reasonable interpretation of Krieg's claims is that they encompass treating asthma wherein an ISS is not co-administered with an antigen. (Paper 50, p. 5, ll. 14-16).

Raz and its expert acknowledge that Krieg's earlier specifications are similar to Krieg's involved specification. (See, e.g., RX 2001, ¶ 141, Paper 50, p. 7, l. 17, to p. 8, l. 4). Raz however, contends that the earlier specifications should be interpreted as not describing a method of treating asthma using an ISS as the specification does not literally state treat asthma by administering an ISS without co-administering an antigen.

Specifically, Raz takes the position that Krieg's '652 and '774 applications either generically refer to methods of treating asthma using an ISS or describe treating asthma by co-administering an ISS with an antigen. (Paper 50, p. 5, l. 28 to p. 6, l. 5). Raz contends that there is not a single instance where Krieg's earlier applications describe using an ISS to treat asthma without co-administering an antigen. (*Id.* at p. 6, l. 5-7). From this interpretation, Raz concludes that Krieg fails to describe a method of treating asthma using an ISS without an antigen. (*Id.* at p. 6, ll. 8-10).

Both the '652 and '774 applications state that an ISS can be administered to treat or prevent the symptoms of asthma. The applications state that the ISS treats or prevents asthma by redirecting an immune response from a Th2 response to a Th1 response. (RX 2006, p. 8, ll. 13-17, RX 2005, p. 10, ll. 18-22). Raz's expert, Dr. Schleimer, testifies that this sentence merely discloses the general concept of administering an ISS to treat or prevent an asthmatic disorder but does not describe any specific method of administering an ISS. (RX 2001, ¶ 120).

Both the '652 and '774 applications teach that the ISS "can be" administered in conjunction with an allergen (antigen) to treat or prevent the occurrence of an allergic reaction associated with an asthmatic disorder. (*Id.*). Raz and its expert, Dr. Schleimer, contend that the "can be" passage informs one of ordinary skill in the art that co-administration of an ISS with an asthma-stimulating antigen could be used to desensitize a subject to treat or prevent an occurrence of an allergic reaction associated with an asthmatic disorder. (Paper 50, p. 7, l. 17 to p. 8, l. 6, RX 2001, ¶ 121).

Raz and its expert conclude that the passage does not describe any specific method of administering an ISS to treat or prevent asthma. (*Id.* at p. 8, ll. 10-11 and RX 2001, ¶ 122). Krieg's expert, Dr. Center, disagrees with Raz and Dr. Schleimer's interpretation of Krieg's earlier specifications. Dr. Center testifies that the "can be" language means what it says. Specifically, Dr. Center testifies that Krieg's specifications inform one of ordinary skill in the art that ISS "may" be administered with an antigen but does not require that the ISS be administered with an antigen in order to be effective. (KX 1057, ¶ 7).

We credit Dr. Center's testimony over that of Dr. Schleimer on the issue of written description. Dr. Center's testimony is more consistent with the plain meaning of the language appearing in Krieg's '652 and '774 specifications. Further, as explained below, Dr. Schleimer's testimony relies in part upon an unsupported theory that one of ordinary skill in the art would have expected that an effective ISS asthma treatment would have required the co-administration of an antigen.

b. Raz Fails to Demonstrate that One Skilled in the Art Would "Expect" That ISS Alone is Ineffective in Treating Asthma

Raz's arguments and Dr. Schleimer's testimony on written description are premised on the theory that one of ordinary skill in the art, at the relevant time, would have expected that a method of treating an asthmatic subject by the administration of an ISS would involve co-administration of an antigen. (Paper 50, p. 6, ll. 11-17 and RX 2001, ¶¶ 103, 105). Raz and Dr. Schleimer however, fail to provide sufficient evidence of this expectation to support such a conclusion and, even if the expectation existed, that the expectation would have led one of ordinary skill in the art to read a requirement into the plain language of Krieg's specification.

Raz and Dr. Schleimer identify 1996-1999 as the relevant time frame for determining the expectation of one of ordinary skill in the art. For example, Raz Motion 3 states:

> In 1996-1999, one of ordinary skill in the art would have expected that a method of treating an asthmatic subject by administration of an ISS would involve co-administration of the particular asthma-stimulating antigen to treat the asthmatic subject.

(Paper 50, fact ¶10, citing Schleimer Declaration, RX 2001, ¶ 103, see also Raz Reply 3, Paper 119, p. 9, ll. 5-10). As discussed below, even if Raz is correct and the state of the art for the '652 and '774 applications extends to what was shown in 1999, Raz has failed to properly take into account Raz's own contemporaneous publication, Broide '98, which reports using an ISS to treat asthma without co-administering an antigen.

Raz relies upon Kline's '96 and '97 abstracts and '98 article as follows for the proposition that:

> Several reports in 1996-1998 that were authored by the named Krieg inventors of the earlier filed Krieg applications indicate that administering ISS without co-administering an antigen is not effective in preventing or treating asthma. See, Facts 37-59. This is further evidence that the earlier-filed Krieg applications did not describe a

broad claim encompassing a method of treating asthma by administering ISS.

(Paper 50, p. 10, ll. 18-22). The Kline '96 and '97 abstracts and the '98 article contain ambiguity and are open to interpretation. As discussed below, we find that the abstracts and article do not establish that one of ordinary skill in the art would understand that ISS without co-administration of an antigen is ineffective in treating asthma.

Kline's '96 abstract describes an experiment where ISS and Schistosome eggs were co-administered to mice, followed by SEA airway challenge. The Kline abstract contains the statement that systemic administration of the ISS alone did not result in significant change in BAL cellularity. This statement can be interpreted in various ways, e.g., the statement could be a reference to a control composition that did not stimulate an immune response in non-sensitized mice. (RX 2001, ¶ 62, KX 1057, ¶ 28).

Kline's '97 abstract, like the '96 abstract, reports testing ISS and Schistosome eggs on mice, followed by subsequent SEA airway challenge. The Kline abstract contains a statement that ISS co-administered with Schistosome eggs, but not ISS alone, lead to decreased airway eosinophilia. As with the '96 abstract, this statement is ambiguous as to the experimental design. (RX 2001, ¶ 72, KX 1057, ¶ 29). One possible interpretation is that the language "but not" ISS refers to a control to demonstrate that the ISS did not appear to effect airway eosinophilia. (RX 2001, ¶ 73).

One of ordinary skill in the art would have understood that Kline's 98 article describes in a detailed manner the experiments reported in Kline's '96 and '97 abstracts. (RX 2001, ¶ 76). Kline's '98 article reports that sensitized mice that were administered ISS and egg had the lowest eosinophil count and thus a marked decrease in the development of airway inflammation. (*Id.* at ¶ 83). In discussing

its findings, Kline's article includes a statement that CpG OND (ISS) alone did not offer significant protection against the development of airway inflammation. (*Id.* at ¶ 81). As with the Kline abstracts, this statement is ambiguous as there is no data to provide context for this statement. (*Id.* at ¶ 83). One of ordinary skill in the art could interpret the statement as a reference to controls wherein an ISS was administered to non-sensitized mice without co-administration of an antigen. (RX 2001, ¶ 83 and KX 1057, ¶ 30).

Kline's '96 and '97 abstracts and '98 article provide ambiguous statements regarding the use of an ISS alone in the treatment of asthma. As the statements are ambiguous, we find that Kline's abstracts and article fail to lead one of ordinary skill in the art to expect that treating asthma with an ISS without the co-administration would be ineffective. (KX 1057, ¶ 27).

Additionally, Raz fails to take into account the contemporaneous statements made in Raz's own co-authored article. Specifically, Raz seeks to rely upon the teachings of Kline's abstracts and article to demonstrate that one skilled in the art would have understood that ISS alone would be ineffective in treating asthma. Raz however, fails to explain how Raz's own contemporaneous statements regarding the abstracts and article are consistent with Raz's post-interference positions.

Raz's coauthored Broide '98 article tested an ISS without co-administration of an antigen. The Broide '98 article does not identify an "expectation" that ISS alone would be ineffective. Rather, Raz's article characterized its ISS test observations as "similar" to those noted in Kline's 98 article, which reported test data for co-administering ISS and antigen. Further, Broide and Raz reported that they had "extended" upon Kline's observations. (RX 2012, p. 7059, col. 2 to 7060, col. 2).

We give greater weight to Raz's contemporaneous 1998 article than Raz's subsequent interference arguments and testimony of Dr. Schleimer. The Broide

'98 article was prepared prior to Raz's involvement in this interference proceeding. The Broide '98 article was presented and addressed to those actually working in the art and was not specifically prepared to advance an interference position. The '98 article stands in a position analogous to that of the affidavit evidence in *In re Carroll*, 601 F.2d 1184 (CCPA 1979). The CCPA gave great weight to an affidavit submitted prior to the making of the claimed invention. As explained by the CCPA:

> Unlike the usual expert opinion, prepared either by the applicant himself, or on his behalf after the controversy has arisen, Dr. Merkal's opinion was formulated prior to the making of the claimed invention. It was therefore completely untainted by either hindsight or bias.

Id. at 1186. Broide's '98 publication stands on a similar footing as it was prepared independent of any involvement in the current interference proceeding and is entitled to greater weight than Raz's current arguments, and the conclusions of its expert as they are made in the context of the interference almost a decade after Broide published.

We credit Raz's contemporaneous statements that its use of an ISS without antigen is an extension of Kline observations. We do not credit Raz and its expert's post-interference contention that one of ordinary skill in the art would have expected that an effective treatment of asthma with ISS would have required the co-administration of an antigen.

Raz has failed to meet its burden of proof and demonstrate that Krieg's earlier filed '652 and '774 applications lack sufficient written description for the treatment of asthma using an ISS without the co-administration of an antigen. Specifically, we credit the testimony of Dr. Center and find that the plain language of Krieg's earlier filed applications reasonably conveys to one of ordinary skill in the art that Krieg invented a method of treating asthma involving the

administration of an ISS where the ISS "can be" co-administered with an antigen. We do not credit Dr. Schleimer's testimony to the contrary as it seeks to read a requirement into Krieg's specifications based on an alleged expectation that is not supported by the record.

4. Krieg's '652 and '774 Applications Teach One of Ordinary Skill in the Art How to Make and Use the Claimed Invention

Raz contends that Krieg lacks § 120 benefit of the '652 and '774 applications as the applications fail to enable a method of administering ISS, without limitation to the administration of an antigen. (Paper 50, p. 4, ll. 20-22). Accordingly, the question presented is whether one of ordinary skill in the art following the teachings contained in Krieg's '652 and '774 application could have made and used the claimed invention without undue experimentation where the sole point of difference in dispute is whether one of ordinary skill in the art could administer an ISS to treat asthma without co-administering an antigen. (Paper 50, p. 15, ll. 18-20).

Raz contends that the state of the art, the breadth of the claims and the lack of direction or guidance presented in the specification demonstrates that undue experimentation would have been required to practice the full scope of Krieg's claims. (Paper 50, p. 14, ll. 12-15). We consider the three cited Wands factors but also consider the level of skill in the art and the quantity of experimentation needed to be performed.

Raz's sole argument as to the breadth of Krieg's claims is that Krieg's claims encompass at least two embodiments: methods of treating asthma by administering an ISS with or without the co-administration of an antigen. (Paper 50, p. 14, ll. 17-23).

We find that the level of skill in the art was high. Specifically, we credit the

testimony of Dr. Schleimer and Dr. Center that a person of ordinary skill in the immunological arts would have an advanced degree, M.D. or Ph.D., in immunology, molecular biology or similar discipline and several years of laboratory or clinical experience with immune responses and/or asthma. (RX 2001, ¶ 16 and KX 1003 at ¶ 10).

We agree with Raz that the state of the art was such that one of ordinary skill in the art would have required experimental test data before definitely concluding that an ISS alone could be used to treat asthma. (RX 2001, ¶ 135). Yet, the test for enablement does not preclude some experimentation only undue experimentation.

Additionally, with respect to the state of the art, Raz does not dispute that those of skill in the art were aware of ISS's. (RX 2001, ¶¶ 53-55). Raz also does not dispute that those of skill in the art were familiar with treating asthmatic subjects. Nor does Raz dispute that those of skill in the art were aware that ISS's had previously been administered to asthmatic subjects. (See, e.g., RX 2001, ¶¶ 59-60).

We find that Raz fails to establish that Krieg provides insufficient guidance to one of ordinary skill in the art. Specifically, Raz fails to state what additional step or teaching was lacking in Krieg such that one of ordinary skill in the art could not practice the claimed invention, absence of co-administering an antigen. At most Raz states that Krieg fails to provide sufficient guidance due to a lack of working examples. (*Id.* at p. 15, l. 18 to p. 16, l. 11). Yet, Raz has failed to establish that Krieg fails to provide sufficient guidance to one of ordinary skill in the art as: 1) ISS's were known compounds, 2) asthmatic subjects were known in the art, 3) Krieg provides an Example 12[4] that reports administering ISS and an antigen in a murine model of asthma, and 4) the sole difference in dispute is

4 For purposes of this decision we treat Krieg Example 12 as prophetic in nature.

whether one skilled in the art could administer the ISS without also co-administering a second compound, an antigen.

Raz does not allege that the quantity of testing was excessive in order to practice the invention. We find that a limited quantity of routine testing was required to establish that an ISS could be used to treat asthma without the co-administration of an antigen. The basis for this finding is Raz' own 1998 publication, Broide '98, which identifies its observations as extending upon Kline's. (RX 2012).

In view of the strong factors in favor of enablement, high level of skill in the art, limited quantity of routine testing necessary to practice the invention, the use of known compounds administered to a known class of subjects, and a prophetic example detailing the administration of the ISS to an asthmatic subject (albeit co-administering an additional compound) we hold that Raz has failed to demonstrate that Krieg's '652 and '774 applications would have required one of ordinary skill in the art to practice the claimed method of treating asthma using an ISS, with or without an antigen.

Raz Motion 3 for judgment on prior art is ***denied***.

C. Krieg Continent Responsive Motion 4: To Add New Claims

Krieg Motion 4 is a contingent motion that seeks to add new claims 104 and 105 to Krieg's involved application. (Paper 79, p. 1, ll. 1-2). Krieg's motion is contingent upon the grant of Raz Motions 1 or 3, which allege that all of Krieg's involved claims are unpatentable to Krieg. Raz Motions 1 and 3 are denied and as such, the contingency has not come to pass. Krieg Motion 4 is dismissed as moot.

D. Raz Substantive Motion 2 for Judgment of No Interference-in-Fact

Raz Substantive Motion 2 requests that judgment be entered that no

interference-in-fact exists between the parties. (Paper 48, p. 1, ll. 2-7). Krieg opposes. (Paper 100, p. 1, ll. 2-10).

Raz contends that Krieg's claims fail to anticipate and/or render obvious Raz's involved claims. Generally, Raz states that its claims treat asthma by administering an immunostimulatory peptide ***without*** administering an antigen. Raz states that Krieg's claims do not recite whether its method of treatment is without an antigen. From this, Raz concludes that Krieg's claims would not have anticipated Raz's method of treatment and further states that administering an immunostimulatory peptide without antigen would not have been obvious to one of ordinary skill in the art. (*Id.* at p. 1, l. 23 to p. 2, l. 14).

The rules specifically provide that an interference-in-fact exists as follows:

> *Interfering subject matter*. An interference exists if the subject matter of a claim of one party would, if prior art, have anticipated or rendered obvious the subject matter of a claim of the opposing party and vice versa.

37 C.F.R. § 41.203(a). Raz does not dispute that Raz's claims would, if prior art, anticipate and/or render obvious Krieg's claims. Accordingly, the issue before us is whether Krieg's claims, ***taken as prior art***, anticipate or render obvious Raz's claims, and vice versa.

1. Krieg Claim 44 Anticipates Raz Claim 17

The plain language of Krieg claim 44 does not require presence of antigen. Raz argues, and Krieg agrees, that Krieg claim 44 is generic with respect to the administration of an ISS with or without antigen. (Paper 48, p. 6, l. 11 to p. 7, l. 3, Paper 100, p. 4, ll. 22-23). Accordingly, there are two options, antigen or no antigen. Here, we find that the small genus of two (with or without antigen) anticipates the species (without antigen). *In re Petering*, 301 F.2d 676 (CCPA

1962) (Prior art reference disclosing limited genus of 20 compounds rendered every species within the genus unpatentable); *In re Schaumann*, 572 F.2d 312 (CCPA 1978) (Prior art embraces very limited number of compounds closely related to one another inevitably leading to the conclusion that the prior art provides a description of those compounds and bars later claim covering those compounds).

Raz Reply 2 contends that one of ordinary skill in the art would not have been able to envisage the administration of an ISS without an antigen. (Paper 118, p. 1, l. 22 to p. 2, l. 6). Raz states that one of ordinary skill in the art could not have envisaged the without co-administration of an antigen species as the art was not predictable and administering an ISS alone was not a known option. (*Id.* at p. 7, ll. 16-23).

Raz's "envisage" argument is not persuasive as one of the only two options of Krieg claim 44 anticipates Raz claim 1. Specifically, Krieg claim 44 requires only the administration of an ISS and make no mention of an antigen. Further, Raz has acknowledged that one of ordinary skill in the art would understand that Krieg's involved claims encompass methods wherein ISS is not co-administered with an antigen. (Paper 50, p. 5, ll. 14-16). Raz's "envisage" argument is in essence an attack on whether one of ordinary skill in the art would have understood that co-administration of an antigen was required for efficacy. Anticipation however, only requires that the suggestions in a reference be enabled and does not require proof of efficacy. *Rasmusson v. SmithKline Beecham Corp.*, 413 F.3d 1318, 1325-26 (Fed. Cir. 2005) ("[A] prior art reference need not demonstrate utility in order to serve as an anticipating reference under section 102.").

Additionally, for purposes of a no interference-in-fact analysis, Krieg's claims are assumed to be *prior art*. 37 C.F.R. § 41.203(a). That is, Krieg's claims are assumed to be described and enabled for their full scope and prior in time to

Raz's claims.

A motion for no interference-in-fact presents a very narrow question: are the parties claiming the same subject matter? A no interference-in-fact motion is not a motion for judgment that an opponent's claims are unpatentable for failure to comply with the written description and enablement requirements. Nor is a motion for no interference-in-fact a motion for judgment that an opponent's claims do not represent prior art to the moving party. These issues are to be raised and considered in separate motions, such as in Raz's Motion 1 discussed above, which requests judgment against Krieg's involved claims for lack of sufficient written description and/or enablement.

Again, both parties agree that one of ordinary skill in the art would have understood that Krieg claim 44 is generic with respect to administration of an antigen, i.e., it encompasses administering an ISS with or without an antigen. Applying the test set forth in 37 C.F.R. § 41.203(a), the full scope of Krieg's claim is presumed to be described, enabled and prior in time to Raz. Krieg's genus encompasses two embodiments and, under the facts before us, the described and enabled genus of two anticipates both species covered by the genus.

Raz Motion 2 for no interference-in-fact is ***denied***.

E. Krieg Substantive Motion 2 for Judgment Based on Lack of Sufficient Written Description and/or Enablement

Krieg Substantive Motion 2 moves for judgment against all of Raz's involved claims alleging that the claims are unpatentable for lack of sufficient written descriptive support and/or enablement. (Paper 34, p. 1, ll. 3-6). Raz opposes. (Paper 101).

Raz's claims are generally directed to a method of treating asthma by administering an immunostimulatory polynucleotide comprising an

immunostimulatory sequence (ISS) to a mammal sensitized to an asthma-stimulating antigen where the polynucleotide is administered without the antigen. (Raz Copy of Claims, Paper 8, Claim 1). Several of Raz's involved claims limit the size of the ISS to at least six nucleotides in length. (*Id.* at claims 2-4, 6, and 17).

Krieg contends that the claims are unpatentable due to their "extreme breadth" in relation to the disclosure contained in Raz's specification. (*Id.* at p. 1, l. 9 to p. 2, l. 2). More particularly, Krieg contends that Raz's claims 1) fail to describe and enable unmethylated ISSs and ISSs of less than six nucleotides in length, 2) fail to describe or enable the claimed immunostimulatory polynucleotides, which can be relatively large and include plasmids of 30,000 nucleotides in length, 3) fail to teach one of ordinary skill in the art to identify the antigens that are excluded from the claims.

1. Findings of Fact

The following findings of fact are believed to be supported by a preponderance of the evidence. These findings are in addition to those discussed above.

a. Raz's Involved '148 Specification

72) Raz's '148 patent issued from application 09/235,742, filed January 21, 1999, which is the date for determining written description and enablement of Raz's involved claims.

73) Raz's '148 patent relates to methods and oligonucleotide compositions for use in reducing or suppressing granulocyte-mediated inflammation and modulating immune responsiveness to an antigen. The main therapeutic goals of Raz's patent are the treatment of inflammation and boosting of the immune responsiveness with

a Th1 phenotype against a sensitizing antigen. ('148 Patent, KX 1001, col. 1, ll. 23-26 and col. 3, l. 66 to col. 4, l. 2).

74) Raz's patent states that an example of a therapeutic use for its invention is the control of asthma. (*Id.* at col. 2, ll. 21-24).

75) The patent states that the invention provides a means to shift a immune response to an antigen away from a Th2 response to a Th1 response. (*Id.* at. col. 2, ll. 35-37).

76) The patent defines the immunostimulatory sequences of the invention as six (6) nucleotides or greater in length. Specifically, the '148 patent states:

> Structurally, ISS-ODN are non-coding oligonucleotides 6 mer or greater in length which may include at least one unmethylated CpG motif.

(*Id.* at col. 8, ll. 31-33).

77) The patent reiterates that the ISS is at least 6 mer in length and goes on to state that one skilled in the art could readily identify ISS's. Specifically, the patent teaches that:

> The core hexamer structure of the foregoing ISS-ODN may be flanked upstream and/or downstream by any number or composition of nucleotides or nucleosides. However, ISS-ODN are at least 6 mer in length, and preferably are between 6 and 200 mer in length, to enhance uptake of the ISS-ODN into target tissues. Those of ordinary skill in the art will be familiar with, or can readily identify, reported nucleotide sequences of known ISS-ODN.

(*Id.* at col. 8, ll. 43-50).

78) Raz's patent states that the ISS can be incorporated into a delivery vector, such as a plasmid. (*Id.* at col. 9, ll. 57-62).

79) A plasmid is a double-stranded circular nucleic acid of restricted size, generally about 1,000 to 30,000 nucleotides in length. (Declaration of Dr. Wallner, KX 1011, ¶ 16 and KX 1019, p. 137, col. 2).

80) Raz Example V provides an example of polynucleotide plasmid (pCMV-LacZ) that contains an ISS. (KX 1001, col. 18, l. 61 to col. 20, l. 2).

81) Raz does not provide an example of a method of treating asthma using a plasmid that contains an ISS but not an antigen. (KX 1011, ¶ 21).

b. Relevant Facts Admitted by the Parties

82) Not all plasmids, or other polynucleotides, containing ISSs with CG nucleotides would be useful in the treatment of asthma. (Krieg Reply 2, Paper 114, ¶ 53).

83) To select other polynucleotides (including plasmids) for insertion of ISSs for use within the scope of Raz's involved claims, one of ordinary skill in the art would have to experiment with each different ISS to determine if it remained immunostimulatory in a particular polynucleotide. (*Id.* at ¶ 57).

84) One of skill would also have to experiment to determine where the ISS should be placed in a particular polynucleotide. (*Id.* at ¶ 58).

c. Testimony of Dr. Barbara Wallner

85) Dr. Wallner testifies that Raz's claims do not limit the upper limit of the length of the immunostimulatory sequence. (KX 1011, ¶ 41).

86) Raz's claimed CG could be located at any position along the length of the immunostimulatory sequence. (*Id.*).

87) Since there are only four types of nucleotides in plasmids (A, C, G, T) there is a high likelihood that C and G will be adjacent to each other, for example there are hundreds of CG-containing sequences in the plasmids pKCB and PCMV. (*Id.* at ¶¶ 29-31 and 37).

88) Plasmids were known in 1997 as having potential use in one of two therapeutic purposes: gene therapy and DNA vaccines. (*Id.* at ¶ 43).

89) The use of plasmids in a mammal for therapeutic purposes was, and *remains*, unpredictable. (*Id.* at ¶ 46).[5]

d. Relevant Cross Examination Testimony

90) On cross-examination Dr. Wallner testified:

> Q. Now, during the time period of, let's say 1997, was it generally understood by those of ordinary skill in the art that when reference was made to CpG-containing immunostimulatory sequences, that those nucleic acid sequences were unmethylated?

5 Most of Dr. Wallner's testimony is directed to the state of the art as of 1997. The date for determining written description and enablement for the involved Raz claims is January 21, 1999. In this respect we focus on Dr. Wallner's testimony that plasmids were and remain unpredictable.

A. I think it – in my opinion it was, since the immunostimulatory properties were seen with DNA extracted from E. coli and oligonucleotides that had not been methylated.

(RX 2042, p. 83, ll. 9-18).

91) On cross-examination Dr. Center testified:

Q. Based on that body of literature, would one of ordinary skill in the art in the 1995 to 1998 time frame have understood a reference to CpG-containing sequences that are immunostimulatory as being unmethylated?
A. Yes.

(RX 2043, p. 70, ll. 2-7).

2. Analysis of Raz's Enablement

a. Raz's ISSs are Unmethylated

Raz's claims require the presence of ISS that is a CG-containing sequence. The claims do not literally state that the CG sequence is unmethylated.

Krieg contends that Raz's claims encompass methylated CG sequences. (Paper 34, ¶ 23). Dr. Wallner testifies in support of Krieg and states that none of Raz's claims require that the CG sequences are unmethylated. (KX 1011, ¶ 10). Krieg contends that Raz's claims lack enablement due to the failure to identify the CG sequence as unmethylated.

Raz's specification identifies the ISS CG sequences as conforming to the unmethylated CpG motif. (KX 1001, col. 8, ll. 31-33). Dr. Wallner and Dr. Center testified on cross-examination that one of ordinary skill in the art would have understood that references to CpG-containing sequences referred to unmethylated sequences. (RX 2042, p. 83, ll. 9-21 and RX 2043, p. 70, ll. 2-7). We hold that one of ordinary skill in the art would understand that Raz's claimed ISS is an

unmethylated CpG containing sequence.

b. Raz's Involved Claims Lack an Enabling Disclosure for Plasmid Polynucleotides

Krieg contends that undue experimentation is required to practice the full scope of Raz's claimed invention. Raz disagrees.

i. Claim Construction

Raz claim 1 recites a method for treating asthma by administering a immunostimulatory polynucleotide comprising an ISS. Raz claim 1, and its dependent claims, do not recite an upper limit on the size of the immunostimulatory polynucleotide or the ISS.

Krieg Motion 2 cites as fact that Raz's polynucleotide can be as large as 1,000 to 30,000 nucleotides in length. Thus, the claim encompasses administration in a plasmid. (Paper 34, ¶ 40, citing KX 1011, ¶ 16 and Raz's '148 patent, KX 1001, col. 9, ll. 57-62). Raz responded to this statement with "Unable to admit or deny." Raz however, does state in its opposition that one of ordinary skill in the art would recognize that plasmids could be within the scope of its claimed invention so long as they contained the recited CpG ISS motif and did not encode an asthma stimulating antigen. (Paper 101, p. 12, ll. 9-11 and p. 14, ll. 10-13).

We provide Raz's claims with their broadest reasonable construction. The plain language of Raz's claims do not limit the upper length of the polynucleotide or ISS and Dr. Wallner has testified that one skilled in the art would understand the nucleotide to encompass plasmids. We find Dr. Wallner's testimony to be consistent with Raz's specification as the specification identifies plasmids as suitable delivery vectors. Accordingly, we hold that Raz's claims encompass, *inter*

alia, administration via plasmid, including those having 30,000 nucleotides.

ii. Undue Experimentation Required to Practice Raz's Method of Treating Asthma with Immunostimulatory Plasmid Polynucleotides

Raz's claimed immunostimulatory polynucleotide comprising an ISS encompasses an enormous number of potential ISS sequences and polynucleotides. There is no defined upper limit on the length of the polynucleotide and ISS. As acknowledge by Raz, its claimed polynucleotide encompasses polynucleotides of great length, including plasmids that contain an ISS and meet the functional limitations of the claims. Plasmids however, can be as long as 30,000 nucleotides. Additionally, the breadth of the claim is compounded by the fact that there is no defined structural limitation on the location and placement of the ISS within the polynucleotide.

The art was unpredictable. Dr. Wallner testifies that the use of plasmids was, and remains, unpredictable for use in the therapeutic treatment of mammals. (KX 1011 at ¶ 46). Accordingly, we find that one of ordinary skill in the art would have been unable to predict whether a particular plasmid having an ISS would be effective in the treatment of asthma absent testing. (See, e.g. KX 1011, ¶ 49).

Raz's specification provides no examples using a plasmid within the scope of its claims for the treatment of asthma. Further, Raz's specification provides little guidance as to which plasmid polynucleotides, and which ISS location on the plasmids would be effective for the treatment of asthma.

One of ordinary skill in the art would be required to conduct a vast number of experiments to make and use the full scope of the claim. Specifically, each plasmid polynucleotide having an ISS in every potential position would have to be tested in a mouse model of asthma in order to determine whether it would be

effective to treat asthma.

We find that the skill in the art was high. Specifically, a person of skill in the art possessed an M.D. or Ph.D. with several years of experience. (RX 2001, ¶ 15).

Balancing the various *Wands* factors we hold that Raz's claims are unpatentable for lack of enablement. Specifically, the shear breadth of the claims, the unpredictability of the art, the lack of working examples and guidance as to which plasmid/ISS polynucleotides would be effective and the vast amount of experimentation necessary leads to a conclusion that undue experimentation is required to practice the full scope of Raz's involved claims.

Raz disagrees that undue experimentation was required and contends that the art described and enabled CpG-containing immunostimulatory plasmids. (Paper 101, p. 14, ll. 4-6). Raz contends that the prior examples of immunostimulatory plasmids combined with its disclosure would have enabled one of ordinary skill in the art to practice the full scope of the claims. Raz however, fails to direct our attention to sufficient and credible evidence to support its conclusion that one skilled in the art could make and use plasmid nucleotide ISSs for the treatment of asthma.

Raz also contends that one of ordinary skill in the art would have been aware of the problems with plasmids (gene therapy and DNA vaccines) and, as a practical matter, may have been less likely to select a plasmid as an immunostimulatory polynucleotide in the context of Raz's involved claims. (Paper 101, p. 13, ll. 11-14). The question presented is whether one of ordinary skill in the art could make and use the full scope of the claim and not only that which they may be more likely to select. Further, Raz's specification explicitly states that the ISS can be incorporated into a delivery vector, such as a plasmid. (*Id.* at col. 9, ll. 57-62). Thus, rather than lead one of ordinary skill in the art away from plasmids, Raz's

specification actually guides one of ordinary skill to employ plasmids.

Raz further contends that one of ordinary skill in the art would understand that the claimed immunostimulatory sequences would ordinarily be oligonucleotides ranging from 6 to 200 nucleotides. Raz's involved claims are not limited to such oligonucleotides.

We hold that Krieg has met its burden of proof that Raz's involved claims lack an enabling disclosure for the full scope of the claims. Krieg Substantive Motion 2 is ***granted***.

F. Krieg Substantive Motion 1 for Judgment Based on Interference Estoppel

Krieg Motion 1 requests that all of Raz's involved claims be held unpatentable based on a lost count interference estoppel arising from prior interference 105,171. (Paper 33). All of Raz's involved claims have been held unpatentable for lack of enablement. Accordingly, we dismiss Krieg Motion 1 as moot.

G. Krieg Substantive Motion 3 for Judgment Based on Prior Art

Krieg Motion 3 alleges that Raz's involved '148 patent is not entitled to 35 U.S.C. §120 benefit of Raz's earlier filed '120 application due to an alleged lack of copendency between the applications. Krieg alleges that, absent benefit of the earlier '120 application, Raz's involved claims are unpatentable over prior art. (Paper 35, p. 2, ll. 1-7). Krieg characterizes the prior art as teaching the administration of a plasmid to treat allergic airway inflammation which is observed in allergic asthma. (Paper 35, p. 18, Declaration of Dr. Center, KX 1003, ¶ 65). Krieg Motion 3 is dismissed as moot as all of Raz's involved claims have already

been held unpatentable to Raz.

H. Raz Contingent Responsive Motion 5 to Revive Parent Application

Raz Motion 5 is contingent upon a finding that Raz's parent '120 application was not copending with Raz's '742 application, which issued as Raz's involved '148 patent. (Paper 91, p. 1, ll. 3-7). Raz Motion 5 is dismissed as moot as the contingency did not come to pass.

I. Raz Contingent Motion 6: Request to Redefine the Interfering Subject Matter by Adding an Application and New Claim to the Interference

Raz requests that the Board exercise its discretion and redeclare the interference by adding Raz's 10/229,208 application to the interference with a new count directed to the subject matter of Raz '208 claim 58 or Krieg claim 44. (Paper 92, p. 1, ll. 3-5 and p. 9, ll. 5-8). Raz Contingent Responsive Motion 6 is contingent upon a finding that all of Raz's presently involved claims are unpatentable to Raz based on the grounds presented in Krieg Substantive Motions 1, 2 and/or 3. (*Id.*). Raz's contingency has come to pass as we granted Krieg Substantive Motion 2 and held that all of Raz's involved claims are unpatentable.

Raz '208 claim 58 reads as follows:

> A method for treating asthma, comprising: administering to a mammal sensitized to an asthma-stimulating antigen an immunostimulatory polynucleotide comprising an immunostimulatory sequence (ISS), wherein the ISS comprises the sequence 5'-cytosine-guanine-3', ***wherein the immunostimulatory polynucleotide has a length of 6 to 200 nucleotides***, wherein the immunostimulatory polynucleotide does not comprise a nucleotide sequence encoding the antigen, and wherein the immunostimulatory polynucleotide is administered without the antigen, including without a polynucleotide encoding the antigen, and in an amount sufficient to treat asthma.

(Paper 92, p. 3, ll. 5-13, emphasis added). Raz claim 58 differs from Raz's involved claims as it limits the upper and lower length of the immunostimulatory polynucleotide. By limiting the upper length Raz has excluded immunostimulatory plasmids from its claims. (Raz Reply 6, Paper 121, p. 4, ll. 21-23).

Raz contends that claim 58 is described, enabled and patentable over the prior art. Raz acknowledges that, assuming Raz's no interference-in-fact motion is denied, that claim 58 would interfere-in-fact with Krieg claim 44. (*Id.* at p. 10, ll. 5-6).

1. Requirements for Adding a Claim

Raz, as moving party, has the burden of establishing that it is entitled to the relief requested. The interference rules provide that a party seeking to add a claim has the burden of showing the patentability of its claims. 37 C.F.R. § 208(c)(1). Consistent with the rules, the Standing Order (Paper 2) requires that a motion to add a claim explain why the proposed claim overcomes the patentability problem.

a. Krieg's Procedural Objection to Raz's Motion

Raz's motion is said to be responsive to Krieg Motions 2 and 3, which allege that Raz' involved claims are unpatentable under §112, 1st paragraph and §102(b). Raz's motion addresses some, but not all, of Krieg's contentions on patentability. Raz justifies its failure to address the additional contentions stating that they have no merit and that there is nothing in the Standing Order or the rules that requires Raz to present a claim to overcome "meritless" arguments. (Paper 121, p. 2, ll. 16-19). The fact that Raz considers Krieg's additional unpatentability contentions meritless does not allow Raz to simply ignore Krieg's contentions for it is the Board, not Raz, that evaluates the merits of the parties' contentions.

Raz, at a minimum, should have commented upon Krieg's additional unpatentability contentions. The record however, is clear as to the parties' positions regarding the patentability of Raz claim 58. Additionally, Krieg has not demonstrated that it was prejudiced by Raz's failure to address the additional contentions. Accordingly, we take no action regarding Raz's alleged non-compliance with the requirements of the Standing Order or the rules.

2. Findings of Fact

The following findings of fact are relevant to the patentability analysis of Raz claim 58, with emphasis on compliance with the written description and enablement requirements of 35 U.S.C. § 112, 1st paragraph.

a. ISSs Were a Recognized Class of Compounds

92) One of ordinary skill in the art as of September 1997 would have been familiar with the concept of ISSs based on the Krieg's published work. (Dr. Wallner Declaration, RX 1011, ¶ 7).

93) Dr. Center testified on cross-examination as follows:

> The reporter: Question: So the recitation, the description of the composition in the Raz claims is sufficient to indicate to one of ordinary skill in the art the class of compositions that are intended to be used in the method; is that your testimony?
> Dr. Center: I think in general, yes, the structure is defined adequately for one - - anyone in the art to have presumed that similar structures would be effective.

(RX 2043, p. 76, l. 17 to p. 77, l. 2).

94) Dr. Center also testified:

> Q. What were you referring to when you said "immunostimulatory nucleic acids"?
> A. I was referring to the general class of DNA that effects immune responses of which the specifics that, Krieg's work, and others were unmethylated CpG containing immunostimulatory.
> Q. So those unmethylated CpG-containing immunostimulatory sequences were a class of compositions that were known in the art as of 1998?
> A. Yes, from published, then oral presentations.
> Q. Do you recall offhand any of the publication that would have described that general class of compositions?
> A. A. There were a number of abstracts submitted to the, I guess then called the American Federation for Clinical Research meetings, for which oral presentations by, I believe either Dr. Krieg or Dr. Kline presented their data. And there were also publications by both Krieg's group and other groups which used those compositions in animal models and in vitro.

(*Id.* at p. 69, l. 4 to p. 70, l. 1.).

95) Dr. Center also testified that one of ordinary skill in the art would have been able to generally predict whether or not a particular CpG nucleotide would have immunostimulatory effects. Specifically, Dr. Center testified:

> Q. Is it true that with respect to any CpG-containing nucleic acid sequence you could determine based on the sequence alone, without the use of these assays, that that sequence was immunostimulatory?
> A. I don't understand how you would -- if you didn't have a marker assay, how you would determine anything.
> Q. Well, there would be a sequence on a piece of paper, you would be able to identify that it is CpG-containing, and based on your observation and analysis of that sequence you could say that is immunostimulatory.
> A. Based upon previously published information that was existing in the literature, one would be able to in general predict whether or not the CpG peptides or CpG nucleotides would have immunostimulatory effects based upon the context in which the CpG was nested.

Q. And this is in the time frame of '95 to '98?
A. Yes.
(*Id.* at p. 72, l. 19 to p. 73, l. 16).

96) Dr. Wallner testified in a prior interference (105,171) that ISSs were known in the art prior to 1996 based upon the work of Krieg and Yamamoto. (KX 2039, ¶ 40).

97) Dr. Wallner's testimony identified Yamamoto and Krieg as teaching that certain sequences, e.g., GACGTC, AGCGCT, AACGTT and AACGTT, were immunostimulatory sequences. (*Id.* at ¶¶ 44-45).

98) One of ordinary skill in the art as of 1996 would have understood that ISSs could be six nucleotides in length. (*Id.* at ¶¶ 40-45).

99) One of ordinary skill in the art was aware of assays and experiments that could identify whether a particular CpG containing polynucleotide was immunostimulatory. (KX 2043, p. 71, l. 7 to p. 72, l. 4, KX2042, p. 51, l. 18 to p. 52, l. 16).

b. ISSs Placed in Plasmids May No Longer Function

100) Dr. Wallner testified on cross-examination that:

Q. So is it your opinion that the immunostimulatory sequences that you identified in the control plasmid, if removed from the plasmid, would not have an immunostimulatory effect?
A. I cannot say that. I don't know that. You would have to actually do the experiment to show that.
Q. Okay. Of the numerous hexamers identified in the first table of Exhibit 1016, which of these did you test for immunostimulatory activity?

A. I tested none. I've never worked with immunostimulatory sequences. And I could not test them unless I do an experiment.

(RX 2042, p. 111, l. 23, to p. 112, l. 11).

c. Asthma Stimulating Antigens Were a Known and Identifiable Class of Compounds

101) Dr. Center testified that "most asthma-stimulating antigens are well known allergens." (Declaration of Dr. Center, KX 1003, ¶ 94).

102) Dr. Wallner testified on cross-examination that:

Q. How would one of ordinary skill in the art determine -- strike that. In the 1997 time period, was there any type of reference that one of ordinary skill in the art could turn to to identify asthma-stimulating antigens?
A. Yes. There are -- there's a list – there was a list at that time already provided through the FDA or NIH, I do not recall now. There's a list of allergens that is publicly available. Or you could have done a publication search through the PubMed to find allergens.
Q. Asthma-stimulating --
A. Yes.
Q. -- allergens? Is there also -- let me get this right -- an entity known as the International Union of Immunological Societies that has an allergen nomenclature subcommittee?
A. Right.
Q. And what's their purpose, what's the purpose of that subcommittee?
A. Allergens have been purified and isolated over the last 20, 30, 40 years and given different names. One of their functions is to – to categorize those allergens and give them a common name so that they can be used by all researchers under the same name.

(RX 2042, p. 69, l. 16 to p. 70, l. 18).

3. Patentability Analysis for Raz '208 Claim 58

Raz Motion 6 does not identify the relevant date for analyzing its compliance with the written description and enablement requirements. Raz's '208 application was filed on August 26, 2002. (RX 2030, p. 1). Raz's Motion and Reply 6 however, direct our attention to the state of the art in 1997, which is the date Raz seeks for purposes of §120 benefit. (Paper 92, Appendix, Paper 121, e.g., p. 7, ll. 5-9 and 14-15). We err on the side of caution and analyze claim 58 of Raz for compliance with the written description and enablement requirements as of 1997.

a. Written Description

Raz claim 58 requires an immunostimulatory polynucleotide having a length of 6 to 200 nucleotides and does not encode an antigen. The immunostimulatory polynucleotide comprises an ISS, which comprises the sequence 5'-cytosine-guanine-3'. Raz '120 and '742 applications define the ISS-ODN as non-coding oligonucleotides 6 mer or greater in length, preferably between 6 and 200 mer in length. The applications also teach that the invention delivers ISS-ODN without co-delivery of an immunizing antigen.

As recognized by Krieg, Raz's "ISS is the whole of or contained in the immunostimulatory polynucleotide that is from 6-200 nucleotides in length, and the ISS must contain a CG. (Paper 108, p. 6, ll. 4-5). Krieg contends that Raz describes only a single immunostimulatory polynucleotide meeting the claim limitations, DY 1018. (*Id.* at p. 6, ll. 9-11). Krieg states that the description of a single sequence does not show possession of the broad scope of immunostimulatory polynucleotide sequences. Krieg also contends that the prior art taught that small sequences of less than eight nucleotides were not active.

Raz has demonstrated that the literal language of its applications supports the claimed immunostimulatory polynucleotide and ISS. Further, Raz has demonstrated that ISSs were a recognized class of compounds whose identity could generally be predicted based upon sequence structure. Raz has also demonstrated that one of ordinary skill in the art knew of assays and experiments to confirm whether a particular sequence was immunostimulatory. Based on the record presented, we find that Raz claim 58 complies with the written description requirement as of the '120 applications September 5, 1997 filing date.

b. Enablement

Raz and Krieg dispute whether claim 58 requires one of ordinary skill in the art to engage in undue experimentation to practice the full scope of the claim, especially with respect to the immunostimulatory polynucleotides and ISSs. This poses a difficult question as there are significant Wands factors favoring both sides.

The factors against enablement include the fact that the art of treating asthma with ISSs was unpredictable and that a significant quantity of experimentation was required to practice the full scope of the invention. Further, Raz failed to provide a working example falling within the scope of its claim.

The factors favoring enablement include the fact that the skill level in the art was high and the state of the art in 1997 was sufficiently developed such that ISS compounds were a generally recognized class of compounds.[6] Further, one of ordinary skill in the art could conduct routine testing on a mouse model of asthma

[6] This is in contrast to the ISS plasmid polynucleotides. *Cf.*, Raz Opposition 2, Paper 101, p. 14, ll. 14-16, ("However, a person would also understand, based on the Raz disclosure and the teachings in the art, that immunostimulatory polynucleotides comprising a CpG-containing ISS would ordinarily be oligonucleotides ranging from 6-200 nucleotides.").

and determine whether a particular immunostimulatory polynucleotide having an ISS was effective.

On balance, we find that the factors favoring enablement outweigh those against. In particular we give more weight to the high level of skill in the art, the fact that routine testing can determine whether a particular ISS is effective for treating asthma, and that claim 58 is essentially directed to the use of known and generally recognizable class of compounds to treat a known ailment. We hold that Raz has met its burden of proof and established that claim 58 meets the enablement requirement as of September 5, 1997.

Additionally, Krieg argues that the claim lacks enablement as Raz fails to provide any description of antigens that stimulate asthma. We disagree as most asthma-stimulating antigens are well known allergens and, at the time of the invention, there was a known, publicly available, list of allergens.

All of Raz's presently involved claims of Raz's '148 patent are unpatentable to Raz. Raz however, has demonstrated on this record that Raz '208 new claim 58 is patentable to Raz.

Based upon the facts presented we exercise our discretion as follows: Raz Contingent Motion 6 is ***granted*** to the extent it requests that we authorize the declaration of an interference between Raz '208 and Krieg '584 directed to the subject matter of Raz '208 claim 58 and Krieg '584 claim 44 but ***denied*** to the extent it requests that the present interference be redeclared with a new count designating Raz's unpatentable claims as well as new claim 58 as corresponding to the new count. Judgment is entered against Raz's involved unpatentable '148 claims.

Although we analyzed claim 58 in terms of the state of the art in 1997, we are not aware of any prior art that renders Raz claim 58 unpatentable should it be determined that Raz is not entitled to 120 benefit of its '120 application. As such,

we did not reach the issue of whether Raz is correct in stating that its petition to revive overcomes the potential lack of copendency between its '120 and '742 applications. Thus, our decision on Raz Motion 6 is without prejudice to Krieg raising the issue of improper copendency during an interference between Raz's '208 application and Krieg's involved 584 application.

J. Raz Motion 4 to Designate Krieg Claims as Corresponding

Raz Motion 4 seeks to designate Krieg claims 46 and 82 to 84 as corresponding to Count 1. (Paper 53). This motion is dismissed without prejudice to Raz requesting that Krieg's claims be designated as corresponding to the count in the interference between Raz '208 and Krieg '584.

K. Raz and Krieg's Motions to Exclude

Raz Miscellaneous Motion 7 seeks to exclude certain exhibits to the extent Krieg relied upon them for the truth of the matter asserted. (Paper 126, p. 1, ll. 4-16). Raz's motion is dismissed as moot as we did not rely upon the exhibits in the disputed manner.

Krieg Miscellaneous Motion 5 seeks to exclude certain exhibits cited in Raz Reply 2 or Raz Reply 4 as they violated the Standing Order prohibition on presenting evidence that could have been presented in the underlying motion. (Paper 190, p. 1, ll. 2-15). Krieg's motion is dismissed as moot as we denied Raz Motion 2 and did not reach Raz Motion 4.

It is:

ORDERED that Raz Motion 1 for judgment based on lack of written description and/or enablement is denied.

FURTHER ORDERED that Raz Motion 2 for judgment of no interference-in-fact is denied.

FURTHER ORDERED that Raz Motion 3 for judgment based on prior art is denied.

FURTHER ORDERED that Raz Motion 4 to designate claims is dismissed as moot.

FURTHER ORDERED that Raz Miscellaneous Motion 5 to revive an application is dismissed as moot.

FURTHER ORDERED that Raz Responsive Motion 6 to add a new application, claim and substitute a count is granted-in-part.

FURTHER ORDERED that Raz Motion 7 to exclude evidence is dismissed as moot.

FURTHER ORDERED that Krieg Motion 1 for judgment based on interference estoppel is dismissed as moot.

FURTHER ORDERED that Krieg Motion 2 for judgment based on lack of enablement and/or written description is granted.

FURTHER ORDERED that Krieg Motion 3 for judgment based on prior art is dismissed as moot.

FURTHER ORDERED that Krieg Responsive Motion 4 to add claims is dismissed as moot.

FURTHER ORDERED that Krieg Miscellaneous Motion 5 to exclude evidence is dismissed as moot.

cc (via electronic filing):

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